

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
DAHNA S. PASTERNAK
ROBINS & PASTERNAK LLP
1731 EMBARCADERO ROAD, SUITE 230
PALO ALTO, CA 94303

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference 8325-0036.60	Date of mailing (day/month/year) 25 MAY 2006
International application No. PCT/US05/03245	International filing date (day/month/year) 03 February 2005 (03.02.2005)
Applicant SANGAMO BIOSCIENCES, INC.	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:
 The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

 When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

 Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 338.82.70.

 For more detailed instructions, see the notes on the accompanying sheet.
2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☒ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.
4. **Reminders**
 Shortly after the expiration of 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

 The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

 Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise, the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

 In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

 See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

8325-0036.60
DOCKETED
Resp Search Report
7/25/06

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer Walter Schlapkohl <i>J. Roberts</i> Telephone No. (571) 272-0500
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Form PCT/ISA/220 (January 2004)

(See notes on accompanying sheet)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 8325-0036.60	FOR FURTHER ACTION <small>see Form PCT/ISA/220 as well as, where applicable, item 5 below.</small>	
International application No. PCT/US05/03245	International filing date (day/month/year) 03 February 2005 (03.02.2005)	(Earliest) Priority Date (day/month/year) 05 February 2004 (05.02.2004)
Applicant SANGAMO BIOSCIENCES, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the Report

a. With regard to the language, the international search was carried out on the basis of:



the international application in the language in which it was filed.



a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☐ Certain claims were found unsearchable (See Box No. II)

3. ☐ Unity of invention is lacking (See Box No. III)

4. With regard to the title,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the abstract,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

a. the figure of the drawings to be published with the abstract is Figure No. _____



as suggested by the applicant.



as selected by this Authority, because the applicant failed to suggest a figure.



as selected by this Authority, because this figure better characterizes the invention.

b. ☒ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/03245

A. CLASSIFICATION OF SUBJECT MATTER

IPC: C12P 19/34(2006.01);C12N 9/22(2006.01)

USPC: 435/91.1,199

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/91.1, 199

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
EAST: PGPUB, USPAT, DERWENT, EPO, JPOElectronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,792,640 A (CHANDRASEGARAN) 11 August 1998 (11.08.1998), see entire document, especially column 3, lines 3-9, 19-22 and 63-65; column 9, lines 37-43 and 50-52; and paragraph bridging columns 14-15.	1-14
Y	PABO, ET AL. Design and Selection of Novel Cys2His2 Zinc Finger Proteins, Annual Review of Biochemistry, 2001, Vol. 70, pages 313-340, see entire document, especially page 313, Abstract; and page 333, first paragraph.	1-14

☐

Further documents are listed in the continuation of Box C.

☐

See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

16 April 2006 (16.04.2006)

Date of mailing of the international search report

25 MAY 2006

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Authorized officer

Walter Schlapkohl

Telephone No. (571) 272-0500

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/03245

Continuation of B. FIELDS SEARCHED Item 3:
MEDLINE

DNA or polynucleotide, zinc finger protein, endonuclease, Fok I

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
DAHNA S. PASTERNAK
ROBINS & PASTERNAK LLP
1731 EMBARCADERO ROAD, SUITE 230
PALO ALTO, CA 94303

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year)

25 MAY 2006

Applicant's or agent's file reference

8325-0036.60

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US05/03245

International filing date (day/month/year)

03 February 2005 (03.02.2005)

Priority date (day/month/year)

05 February 2004 (05.02.2004)

International Patent Classification (IPC) or both national classification and IPC

IPC: C12P 19/34(2006.01);C12N 9/22(2006.01)

USPC: 435/91.1,199

Applicant

SANGAMO BIOSCIENCES, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Date of completion of this
opinion

16 April 2006 (16.04.2006)

Authorized officer

Walter Schlapkohl

Telephone No. (571) 272-0500

DOCKETED

8325-0036.60
Resp w/o (chit must
be filed w/
resp.)

8/25/06

✓

Form PCT/ISA/237 (cover sheet) (April 2005)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US05/03245

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed
☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☐ a sequence listing
☐ table(s) related to the sequence listing

b. format of material

- ☐ on paper
☐ in electronic form

c. time of filing/furnishing

- ☐ contained in the international application as filed.
☐ filed together with the international application in electronic form.
☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US05/03245

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>1-14</u>	YES
	Claims <u>NONE</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-14</u>	NO
Industrial applicability (IA)	Claims <u>1-14</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-14 lack an inventive step under PCT Article 33(3) as being obvious over Chandrasegaran (US Patent 5,792,620) in view of Pabo et al (Annual Review of Biochemistry 70:313-40, 2001). Chandrasegaran teaches a method for cleaving cellular chromatin in a region of interest, the method comprising: selecting the region of interest, providing a first and second zinc finger binding domain which binds to a first and second nucleotide sequence in the region of interest, expressing a first and second fusion protein in a cell, wherein the fusion proteins are comprised of a first and second zinc finger binding domain and a first and second cleavage half-domain, wherein the first fusion protein binds to the first nucleotide sequence and the second fusion protein binds to the second nucleotide sequence, and further wherein said binding positions the cleavage half-domains such that the cellular chromatin is cleaved in the region of interest (see entire document, especially column 3, lines 3-9, 19-22, and 63-65; column 9, lines 37-43 and 50-52; and paragraph bridging columns 14-15). Chandrasegaran further teaches such a method wherein the first and second cleavage half-domains are from the same Type IIS endonuclease, *Fok I* (see, e.g., column 9, lines 38-43 and 50-52; column 10, lines 29-35).

Chandrasegaran does not teach such a method wherein the zinc finger binding domains are engineered to bind to a first and second nucleotide sequence in the region of interest.

Pabo et al teach a method of engineering a zinc finger protein to bind to a first and second nucleotide sequence of interest (see entire document, especially page 313, Abstract and page 333, first paragraph). Pabo et al teach that engineered zinc finger domains can be attached to call manner of other protein domains, including the *Fok I* cleavage domain, in order to create a chimeric protein of interest (page 333, first paragraph). Pabo et al also teach that zinc finger fusion protein engineering is "likely to stimulate broader progress in the development of human gene therapy and in medical applications of our new knowledge of the human genome" (page 336, second paragraph).

It would have been obvious for one of ordinary skill in the art to combine the methods of Chandrasegaran and Pabo et al because both Chandrasegaran and Pabo et al teach methods of designing zinc finger domain-*Fok I* cleavage domain fusion proteins. Furthermore, Pabo et al teach that zinc finger fusion protein engineering is "likely to stimulate broader progress in the development of human gene therapy and in medical applications of our new knowledge of the human genome."

One of ordinary skill in the art would have been motivated to combine the methods of Chandrasegaran and Pabo et al because Chandrasegaran teaches a method for making a zinc-finger domain-*Fok I* cleavage domain fusion protein for use as a site-specific endonuclease and Pabo et al teach methods for engineering such a protein to bind to a specific DNA sequence.

Based on the prior art and the high skill level of one of ordinary skill in the art, there would have been a reasonable expectation of success when combining the methods of Chandrasegaran and Pabo et al.

Claims 1-14 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

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PATENT COOPERATION TREATY

WO 2005/084190
PCT/US2005/003245

From the INTERNATIONAL BUREAU

PCT

SECOND AND SUPPLEMENTARY NOTICE
INFORMING THE APPLICANT OF THE
COMMUNICATION OF THE INTERNATIONAL
APPLICATION (TO DESIGNATED OFFICES
WHICH APPLY THE 30 MONTH TIME
LIMIT UNDER ARTICLE 22(1))

(PCT Rule 47.1(c))

To:

PASTERNAK, Dahna S.
ROBINS & PASTERNAK LLP
1731 Embarcadero Road, Suite 230
Palo Alto, ca 94303
ETATS-UNIS D'AMERIQUE

DOCKETED *DSF*

Date of mailing (<i>day/month/year</i>) 08 June 2006 (08.06.2006)		
Applicant's or agent's file reference 8325-0036.60		
IMPORTANT NOTICE		
International application No. PCT/US2005/003245	International filing date (<i>day/month/year</i>) 03 February 2005 (03.02.2005)	Priority date (<i>day/month/year</i>) 05 February 2004 (05.02.2004)
Applicant SANGAMO BIOSCIENCES, INC. et al		

1. **ATTENTION:** For any designated Office(s), for which the time limit under Article 22(1), as in force from 1 April 2002 (30 months from the priority date), **does not apply**, please see Form PCT/IB/308(First Notice) issued previously.

2. Notice is hereby given that the following designated Office(s), for which the time limit under Article 22(1), as in force from 1 April 2002, **does apply**, has/have requested that the communication of the international application, as provided for in Article 20, be effected under Rule 93bis.1. The International Bureau has effected that communication on the date indicated below:
15 September 2005 (15.09.2005)

AU, AZ, BY, CN, CO, DZ, EP, HU, KG, KP, KR, MD, MK, MZ, NA, PG, RU, SY, TM, US

In accordance with Rule 47.1(c-bis)(i), those Offices will accept the present notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

3. The following designated Offices, for which the time limit under Article 22(1), as in force from 1 April 2002, **does apply**, have not requested, as at the time of mailing of the present notice, that the communication of the international application be effected under Rule 93bis.1 :

AE, AG, AL, AM, AP, AT, BA, BB, BG, BR, BW, BZ, CA, CR, CU, CZ, DE, DK, DM, EA, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KZ, LC, LK, LR, LS, LT, LV, MA, MG, MN, MW, MX, NI, NO, NZ, OA, OM, PH, PL, PT, RO, SC, SD, SG, SK, SL, SM, TJ, TN, TR, TT, UA, UZ, VC, VN, YU, ZA, ZW

In accordance with Rule 47.1(c-bis)(ii), those Offices accept the present notice as conclusive evidence that the Contracting State for which that Office acts as a designated Office does not require the furnishing, under Article 22, by the applicant of a copy of the international application.

4. TIME LIMITS for entry into the national phase

For the designated or elected Office(s) listed above, the applicable time limit for entering the national phase will, **subject to what is said in the following paragraph**, be **30 MONTHS** from the priority date.

In practice, **time limits other than the 30-month time limit** will continue to apply, for various periods of time, in respect of certain of the designated or elected Office(s) listed above. For **regular updates on the applicable time limits** (30 or 31 months, or other time limit), Office by Office, refer to the *PCT Gazette*, the *PCT Newsletter* and the *PCT Applicant's Guide*, Volume II, National Chapters, all available from WIPO's Internet site, at <http://www.wipo.int/pct/en/index.html>.

It is the applicant's **sole responsibility** to monitor all these time limits.

RECEIVED

JUN 16 2006

ROBINS & PASTERNAK LLP

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Yoshiko Kuwahara
Facsimile No.+41 22 740 14 35	Facsimile No.+41 22 338 90 90